Correlation of High Seawater Temperature with *Vibrio* and *Shewanella* Infections, Denmark, 2010–2018

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During 2010–2018 in Denmark, 638 patients had *Vibrio* infections diagnosed and 521 patients had *Shewanella* infections diagnosed. Most cases occurred in years with high seawater temperatures. The substantial increase in those infections, with some causing septicemia, calls for clinical awareness and mandatory notification policies.

Tibrio and Shewanella spp. bacteria cause a variety of human infections, including wound infections, ear infections, septicemia, and gastroenteritis (1). Domestically acquired Vibrio and Shewanella infections occur only sporadically in countries in northern Europe because the coastal seawater temperature tends to be too cold to support growth and high bacterial pathogen concentration levels (2,3). However, the warming of low-salinity coastal waters of the Baltic Sea has promoted the growth of Vibrio and Shewanella spp. and consequently increased the risk of disease for humans exposed to such seawater (4). In the unusually warm summer of 1994 in Denmark, several *V. vulnificus* and *S.* algae infections were seen among patients who reported bathing in seawater (5,6). Furthermore, during 2014– 2018, more than 1,055 cases of vibriosis were reported in northern Europe countries, including Denmark (7).

Considering the annual increase in infections during recent summer seasons in Denmark and the recurring heatwaves across Europe, this emerging public health threat requires more investigation to provide

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decision-makers with evidence for action. The aim of our nationwide study was to describe the distribution of *Vibrio* and *Shewanella* infections in Denmark during 2010–2018 and investigate a possible correlation between infections and sea surface temperature.

The Study

We studied cases of Vibrio and Shewanella infections during 2010–2018 in the summer months in Denmark (June to August); in the decade spanning 2010-2020, 2018 was the warmest registered summer in the country. We obtained information about the cases from the Danish Microbiology Database, a national database containing all clinical microbiology reports from Denmark (8). We extracted identification results, confirmed by matrixassisted laser desorption/ionization time-of-flight mass spectrometry, on Vibrio and Shewanella spp. cultured from blood, wound swabs, deep soft tissue, ear, trachea, urine, and feces as well as information about date of sampling. We also extracted the person identification number of each patient studied from Denmark's Central Person Registry (CPR) (9). Clinical patient information was not available, but sample types were used as a proxy for type of infection. We registered cases by month per patient (Appendix 1, https://wwwnc.cdc.gov/ EID/article/29/3/22-1568-App1.pdf). We counted the number of cases by calendar year and stratified them by the genus of isolated bacterial pathogen. Using the CPR number, we eliminated duplicate positive results. By linking to data from the CPR register, we retrieved information on address of residence for each case at the time of sampling. We performed geomapping and geocoding in QGIS 1.8.0 Lisboa (https://www.qgis.org) for the spatial analysis of Shewanella and Vibrio cases and plotting of number of infections per municipality, which we further interpreted based on seawater salinity in the mapped areas. We obtained sea surface temperatures of the coastal waters of Denmark during summer from the Danish Meteorological Institute (Appendix 1; Appendix 2, https://wwwnc.cdc.gov/EID/article/29/3/22-1568-App2.xlsx). We performed the Pearson correlation test in R version 4.2.1 (The R Foundation for Statistical Computing, https://www.r-project.org) to determine correlation between annual summer seawater temperatures and number of *Vibrio* and *Shewanella* cases.

We found a positive correlation between average summer seawater temperatures ($15^{\circ}\text{C}-22^{\circ}\text{C}$) and the number of cases of *Vibrio* (29–172) and *Shewanella* (18–134) infections diagnosed in Denmark during 2010–2018 (p<0.0001; Figure 1, panels A, B). Results showed a higher number of infections during warmer summers compared with colder summers. Ear infections (n = 595) and wound infections (n = 424) were the most frequent clinical manifestations (Table); *V. alginolyticus* and *S. algae* were predominant in ear infections. *V. parahaemolyticus* was the most frequently isolated from wounds (n = 103, 24%), *V. vulnificus* (n = 14, 36%) and *S. putrefaciens* (n = 10, 26%) were

predominant in septicemia cases, and *S. putrefaciens* was the species most associated with deep soft tissue infections (Table). Clinical manifestations varied by bacterial species. More than one third of *V. vulnificus* infections manifested as septicemia, supporting evidence of the high virulence of this species (10–12).

Vibrio and Shewanella infections increased during every summer in the study period. The summers of 2014 and 2018 were characterized by particularly high sea surface temperatures and showed an association to higher incidence in infections (Figure 1, panels A, B). In all studied years, the frequency of Vibrio and Shewanella spp. infections increased beginning in week 23, reaching a peak in the warmest months (July and August), followed by a tail of decreasing number in subsequent months (Appendix 1 Figure, panel A). A recent study on 2018 data alone reported that most human vibriosis cases reported in the Nordic region were likely linked to exposure to the warm seawater that year (7). We found that infections were more prevalent in men and boys 10–19 years of age and in elderly

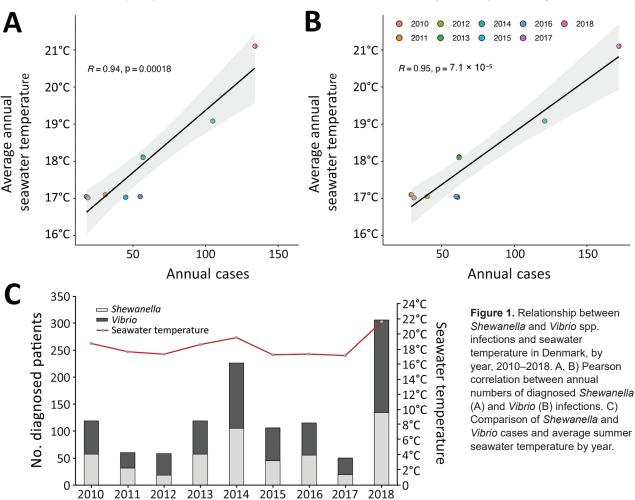


Table. Distribution of species per type of Vibrio and Shewanella infections, Denmark 2010–2018*

	Type of manifestation or site of infection, no. (%)							
	'	Wound and			Deep soft	Respiratory		
Bacterial species	Ear	shallow soft tissue	Septicemia	Feces†	tissue	tract	Urine	Other
Shewanella algae	99 (16.6)	82 (19.3)	4 (10.3)	NA	3 (12.5)	6 (30)	1 (7.7)	2 (9.5)
S. putrefaciens	86 (14.5)	80 (18.9)	10 (25.6)	NA	12 (50)	7 (35)	8 (61.5)	10 (47.6)
Shewanella spp.‡	58 (9.7)	41 (9.7)	1 (2.6)	NA	1 (4.2)	6 (30)	2 (15.4)	2 (9.5)
Total Shewanella	243	203	15	NA	16	19	`11	14
Vibrio alginolyticus	248 (41.7)	72 (17)	2 (5.1)	2 (8.7)	4 (16.7)	1 (5)	0	4 (19)
V. cholerae	12 (2)	1 (0.2)	O	4 (17.4)	0	Ò	0	1 (4.8)
V. fluvialis	9 (1.5)	3 (0.7)	1 (2.6)	4 (17.4)	0	0	0	0
V. parahaemolyticus	36 (6.1)	103 (24.3)	5 (12.8)	9 (39.1)	2 (8.3)	0	0	1 (4.8)
V. vulnificus	2 (0.3)	11 (2.6)	14 (35.9)	1 (4.3)	2 (8.3)	0	2 (15.4)	0
Vibrio spp.‡	45 (7.6)	31 (7.3)	2 (5.1)	3 (13)	O	0	0	1 (4.8)
Total Vibrio	352	221	24	23	8	1	2	7
Total	595	424	39	23	24	20	13	21

*NA, not applicable.

‡Not identified to species level.

persons, 60–80 years of age (Appendix 1 Figure, panel B). We suspect that those results are likely because active adolescents may have scratches or wounds while performing recreational water activities (e.g., swimming, rowing, windsurfing, or fishing) and because of the vulnerability of elderly persons in general.

We found a marked geographic distribution in results obtained from 2018, when most cases were in persons who lived near coastal areas with brackish waters characterized by low saline levels (<30 parts per thousand; Figure 2) (13). In contrast, along the west coast of Jutland, where the salinity of the North Sea is high

and the water colder, the frequency of infections was lower. This difference suggests that increased temperature of low-salinity water favors the growth of *Vibrio* and *Shewanella* bacteria. It is important to consider that the association between place of residence and number of cases is challenged because geographic distances are short in Denmark and multiple exposures at different geographic sites during a summer season are to be expected. The lack of information on prior seawater exposure and information on international travel for each case is a limitation for the correlation between number of *Vibrio* and *Shewanella* infections and seawater exposure.

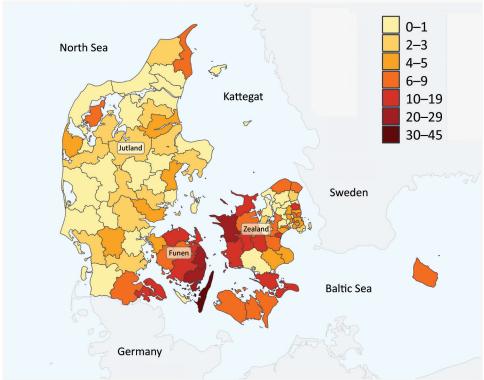


Figure 2. Number of cases of *Shewanella* and *Vibrio* spp. infection (n = 98), by municipality, Denmark, 2018.

[†]S. algae, S. putrefaciens, S. spp. found in feces samples (n = 24) were excluded from all analyses.

Nevertheless, the observed geographic distribution of cases and the presented correlation between the number of cases in cold and warm summers strongly supports a relationship between higher-temperature/low-saline seawater exposure and risk of infection.

Conclusions

In this nationwide study, we show a correlation between number of Vibrio and Shewanella human infections and coastal summer water temperature in Denmark during 2010-2018. In addition, we were able to map residency of most cases to geographic areas with coastlines of low salinity. A combination of climate change effects (i.e., increasing coastal sea surface temperature at higher latitudes during summer) and a more elderly population indicates the need for increased awareness of the risk of these emerging infections and their public health impact. Rising temperatures will lead to an increase in burden of disease for these marine infections in an expanding area of the northern hemisphere (14). We propose that persons in Denmark who are exposed to seawater in summer should consider covering open wounds with a waterproof bandage, particularly the elderly and immunocompromised. We also recommend that persons thoroughly wash new cuts exposed to seawater and inform healthcare professionals of recent seawater exposure when seeking medical attention. Persons with defected eardrums should use earplugs. Our study lends support to categorizing all Vibrio and Shewanella infections in humans as mandatory notifiable diseases in Denmark and other countries in Europe that have seawater borders to monitor the incidence of these infections.

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This study was conducted based on administrative register data. According to Denmark law, ethics approval is not needed for such research. The study is covered by the legal acts regulating national surveillance of infectious diseases.

About the Author

Dr. Hounmanou is a postdoctoral fellow at the University of Copenhagen. He conducts research in microbial genomics on human pathogens that arise from animals and the aquatic environment and addresses questions related to climate change implications on disease transmission between humans and waterbodies, such as cholera and other *Vibrio* infections.

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Appendix 1

Materials and Methods

Description of the study area and framework

Denmark is a Nordic European country consisting of a peninsula, Jutland, and an archipelago of 78 inhabited islands. The sea surrounding the major islands e.g., in the Baltic Sea, have saline levels of between 10–20 parts per thousand. Denmark has a population of 5.8 million and is divided into five administrative Regions, which are further subdivided into 98 municipalities. The administrative Regions are administrating the health care system, which is tax-funded. There are currently ten clinical microbiological laboratories throughout the country, responsible for all clinical microbiology diagnostic services. Clinical microbiology laboratory results have since 2010 been recorded systematically in the national Danish Microbiology Database (MiBa) (1). A unique person identification number (Central Person Registry, CPR) enables linkage between health and administrative register data and identifies all Danish residents (2).

Data extraction

The study period was from 2010 to 2018. From MiBa, we searched for and extracted information on all bacterial cultures done for *Vibrio* spp. and *Shewanella* spp. These bacterial culture data were registered in MiBa following standardized microbiological procedures across all clinical laboratories in the country (Appendix 2, Table 1). The extracted data included date of sampling; anatomic sampling site of the patient, CPR number of person tested and test results. The quality of data was validated by comparison with local clinical microbiology laboratory

databases at the Departments of Clinical Microbiology at Herlev and Gentofte Hospital, Odense University Hospital and Zealand University Hospital. This comparison confirmed that patients registered in the laboratory systems had also been correctly identified in MiBa (data not shown). Information on municipality of residence was obtained from the Central Person Registry (2). Demographic data, i.e., size of the Danish population by sex, age, municipality and year, were obtained from Statistics Denmark (3). As cases were extracted from the MiBa database, information on recent seawater exposure or foreign travel were not available.

Oceanographic data mainly seawater temperature characterizing the summer periods in Denmark (July to August) was obtained from the Danish Meteorological Institute (https://confluence.govcloud.dk/display/FDAPI/Oceanographic+Observation). All measurements performed within the study period were from all inner water sites, i.e., from the southwestern part of the Baltic Sea, the Belt Sea, the sound and Kattegat and were obtained at depths of 0.1 and 0.2 m. The average annual summer temperature was calculated, disregarding the time of the day of the measurement and the varying number of measurements from each seawater site (Appendix 2, Table 2).

Data analysis

The CPR number, allowing for elimination of duplicate positive test results, identified individual cases. *Shewanella* (*S. algae*, *S. putrefaciens*, *S.* species) found in feces samples (n = 24) was excluded from all analyses. We counted cases by calendar year and pathogen genus, i.e., if the same individual was found positive several times per year with either *Vibrio* or *Shewanella* this was recorded as one case only (Appendix 1 Table). If a person had more than one sample taken – then infection was counted by the first date. Pathogen genus is equivalent to the entries listed (Table). That is, a patient may e.g., have both a *Vibrio* spp. case and a *V. fluvialis* case within the same calendar year. In the cases of polymicrobial infections with additional non-*Vibrio/Shewanella* species, only the *Vibrio* and *Shewanella* were counted are presented in this study.

The Pearson correlation test was performed in R version 4.2.1 to determine the correlation between variations of annual summer seawater temperature on the annual number of cases of *Vibrio* and *Shewanella* infections.

Geo mapping and geocoding QGIS 1.8.0_Lisboa (<u>www.qgis.org</u>) was used for the spatial analysis of *Shewanella* and *Vibrio* cases and plotting of number of infections per municipality. A geographical database with

municipality borders in vector format (SHP file) was obtained from the Danish Geodata Agency (GST). Cases were geocoded using the Central Population Registry (CPR registry) and the geocoding of addresses from GST. The address data used for the study originated from the Danish Geodata Agency and were built on Official Standard Addresses and Coordinates (OSAK). Addresses were joined to cases based on the date of the date of sampling.

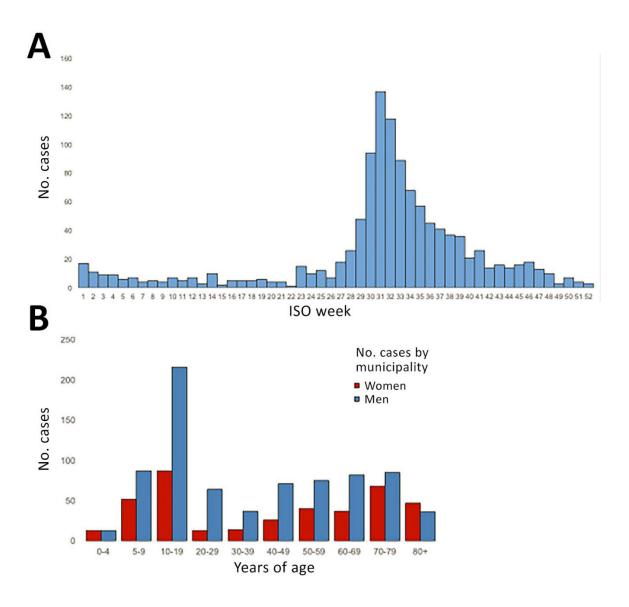
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Appendix 1 Table. Population flowchart

Source	Number of samples	Exclusion
epiMIBA extract (Shewanella, Vibrio)	1456	
Sample date 2010–2018, outside of interval		11
Organism not correctly identified		1
CPR No not valid		24
Shewanella in fecal samples		24
Sample type not relevant		10
Population I	1386	
Address not available in CPR		5
Population II	1381	
Number of cases (patient year organism)	1159	



Appendix 1 Figure. Number of patients diagnosed with *Vibrio* spp. and *Shewanella* spp. per ISO week number (panel A) and by sex and age group (panel B) in Denmark during 2010–2018.